Magnetic Resonance Imaging from the Transcriptomic Perspective

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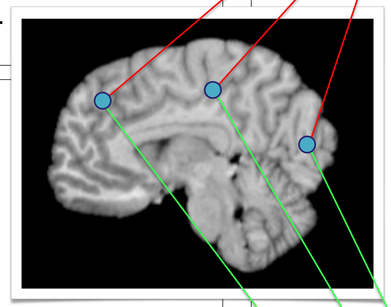
Introduction

In this study, associations between spatially resolved gene expression data and brain imaging data are analyzed. We employ data from the multimodal Allen Human Brain Atlas data set to investigate the transcriptomic associations of the T1-/T2-weighted ratio MRI, which has been proposed as a measure of cortical myelin content. Enrichment analysis using a variety of gene sets can provide evidence regarding the molecular basis of this claim.



Methods

Allen Human Brain Atlas

- 6 brains, 5 male and 1 female, aged 24-57
- 64k Agilent microarray expression data
- Analysis focused on cortex (197–543 samples per brain)
- T1- and T2-weighted MRIs using 3T scanners

Gene Ontology Enrichment Analysis

- Area under the receiver operating curve (AUC) values were generated for 5,909 Gene Ontology groups (10-200 genes each)
- Including 8 myelin-related groups

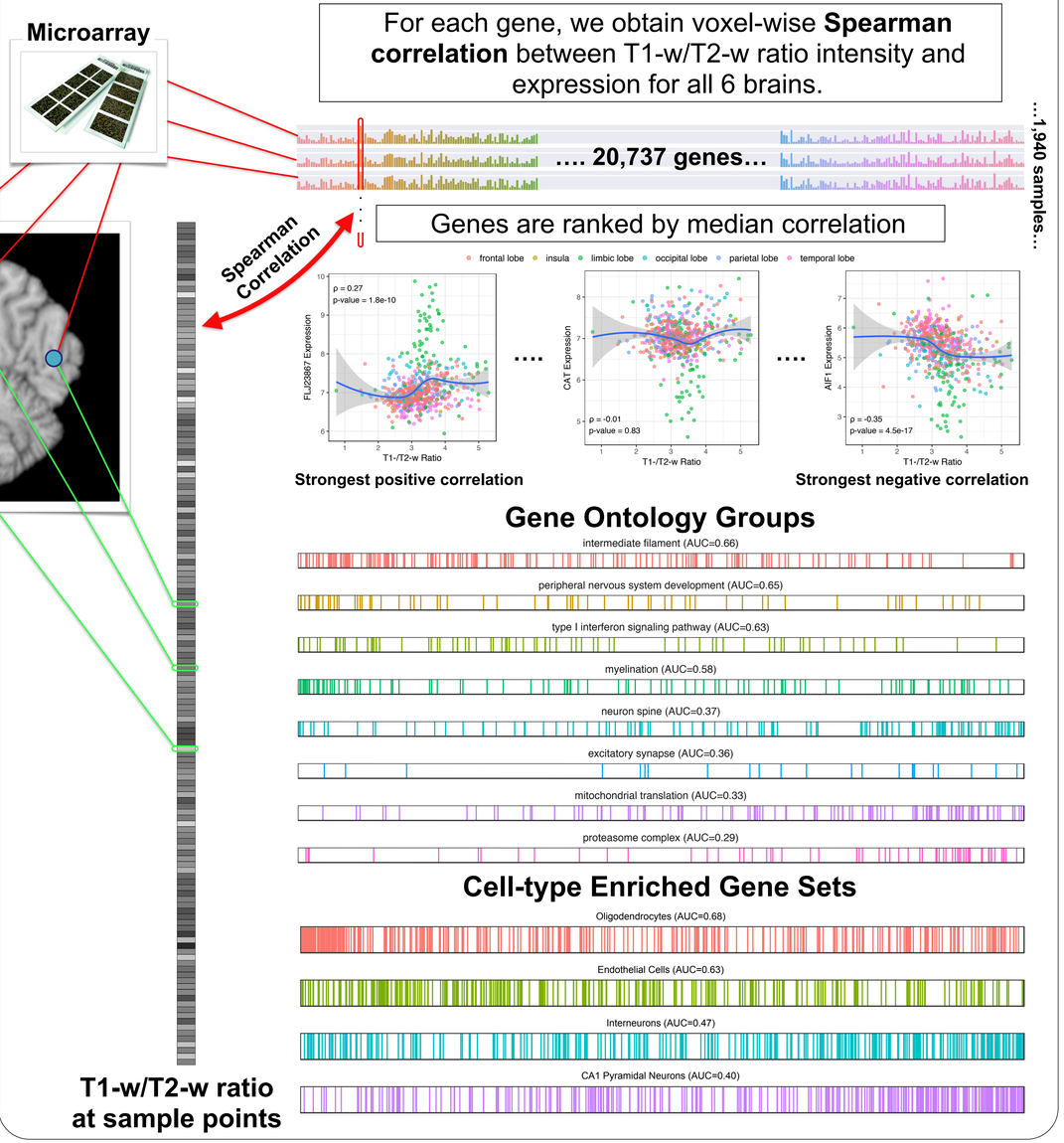
Cell-type Enriched Genes

- We repeated the enrichment analysis for 13 sets of genes that are highly expressed in specific neural cell types (mouse and human)

Phenocarta Analysis

- Enrichment analysis repeated for gene sets corresponding to 1,177 disease phenotypes

Data Flow



Results

- Oligodendrocyte marker genes are positively enriched, while neuron marker genes are negatively enriched
- Five of eight myelin-related GO groups were found to be significantly enriched
- Several diseases related to abnormal myelination are enriched in full brain analyses:
  - Behcet's disease (AUC=0.64, $p=2x10^{-4}$)
  - Angelman syndrome (AUC=0.095, $p=6x10^{-4}$)

A positive correlation is found between cortical T1-w/T2-w intensity and axon caliber genes

- Neurofilament genes are correlated with T1-w/T2-w ratio in order of decreasing chain weight
  - Heavy, $\rho=0.13$, $p=4x10^{-11}$
  - Medium, $\rho=0.10$, $p=2x10^{-4}$
  - Light, $\rho=0.07$, $p=3x10^{-6}$
- Axon caliber is known to be a determinant of myelination

T1-w/T2-w ratio intensity is linked to expression of genes related to the IFN-β signaling pathway, which is implicated in MDD.

- Type 1 Interferon Signaling Pathway (AUC=0.63, $p=4x10^{-3}$)

Conclusion

The **T1-w/T2-w ratio is linked to myelination by several genome-wide enrichment analyses**, providing support for its interpretation as a **myelin sensitive image.** Expression of genes associated with filaments, excitatory synapses, and mitochondria are also correlated with the T1-w/T2-w ratio.

References

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